

DESCRIPTION

5

NOVEL COMPOUNDS FOR TREATMENT OF CARDIAC
ARRHYTHMIA, SYNTHESIS, AND METHODS OF USE40
9/22/04Cross-Reference to Related Application(s)

This application is a continuation application of co-pending application Serial No. 10/319,073, filed December 10, 2002; which claims the benefit of provisional patent application Serial No. 60/339,898, filed December 10, 2001, which is hereby incorporated by reference in its entirety.

Background of Invention

Congestive heart failure (CHF) is a disease affecting approximately 2% of the population of the United States (Sami, M.H. [1991] J. Clin. Pharmacol. 31:1081). Despite advances in the diagnosis and treatment of CHF, the prognosis remains poor with a 5-year mortality rate higher than 50% from the time of diagnosis (McFate Smith, W. [1985] Am. J. Cardiol. 55:3A; McKee, P.A., W.P. Castelli, P.M. McNamara, W.B. Kannel [1971] N. Engl. J. Med. 285:1441). In patients with CHF, the rate of survival is lowest in those patients with severe depression of left ventricular function and patients who have frequent ventricular arrhythmias. Patients with ventricular arrhythmias and ischemic cardiomyopathy have an increased risk of sudden death. The presence of ventricular tachycardia in patients with severe CHF results in a three-fold increase in sudden death compared to those without tachycardia (Bigger, J.T., Jr. [1987] Circulation 75 (Supplement IV):28). Because of the high prevalence of sudden unexpected death in patients with CHF, there has been a growing interest in the prognostic significance of arrhythmias in these patients.

Several compounds have been used in the management of cardiac arrhythmias in patients with congestive heart failure. Unfortunately, anti-arrhythmic drug therapy has been disappointing. The efficacy of anti-arrhythmic drugs markedly decreases as left ventricular function declines, such that only a small fraction of patients with CHF are responsive to anti-arrhythmic therapy. No anti-arrhythmic drug has prevented